

## **Approach to Tremor for the Primary Care Physician**

Hi I'm going to talk with you today about the approach to tremor. I'm going to focus on the most common types of tremor and just kind of go through some general things in terms of recognizing tremor and then also discuss treatment of some of the most common forms of tremor. So just to go through it I'm going to classify tremor and then talk about essential tremor. I'm going to briefly talk about medication and toxic induced tremor and give you some resources to utilize for those types of tremor. Then we'll talk about rest tremor in Parkinson's disease and finally dystonic tremor. So tremor is a rhythmic mechanical oscillation of at least one functional body region. The important things in terms of looking at tremor, one is to know what position activates the tremor most. So whether a tremor is most prominent at rest or at action, such as postural which would just be holding the hands in a certain position, kinetic which would be with a movement, and tension so if it's as if someone is reaching a target, and then task specific tremors are important to know about too. So someone gets a tremor, for example, when they just write and otherwise they don't have a tremor, that can be important. So a rest tremor occurs when a part of the body is not voluntarily activated and the tremor is occurring. It tends to often diminish or disappear when someone moves their hand. For example the hand is the most common place to see it. So in someone with Parkinson's they may have their hand shaking as it's resting in their lap, they lift it up and the tremor's gone. Sometimes it will re-emerge. They'll lift it up, the tremor will be gone and then it will gradually come back. Action tremor occurs most common with voluntary action. It includes postural, isometric, or kinetic. Postural is just holding it. Posture isometric is pushing against a force and then kinetic is actually with a movement. So this is the postural. She's just holding her hands up against gravity. Isometric is as I said, it's kind of pushing against something. I think everyone's had this experience lifting weights or something where their pushing against something heavy and they get a little bit of a tremor. Kinetic occurs with voluntary movements. The reason I've shown a pouring motion here is because we'll check a cup pour to look for kinetic tremor. You can have someone pour water from one cup to another. Intention tremor is a type of kinetic tremor and it has an increased amplitude at a goal directed target. So when you have someone do finger to nose, as they reach your finger they may get more tremor, as they get towards their nose they may get more tremor and that would be an intention tremor. Then task specific tremors may occur with just a specific action as I've said. Writing is the most common area where they see this. Other things to assess in terms of tremor are where the tremor is. Is it in the head, chin, hands, leg? This can really help in distinguishing the etiology of the tremor. Then the activation conditions which I already talked about, and then the frequency. I think this is less helpful and often kind of difficult to tell, but something you get used to if you've seen more tremors. I think the area and the activation conditions are the most important. Other things that you want to look at in the physical exam, and these are really largely to look for Parkinson's in other disorders in someone who has a Parkinson's rest tremor as opposed to someone who has an essential tremor who shouldn't really have a lot of other features. So you want to see if they have increased tone which would be present in Parkinson's. If they have slowness,

again or Bradykinesia which would be present in Parkinson's. If they have Dystonia, so an abnormal posturing of the limb or the head if it's involved in the tremor, and this would lead you towards a dystonic tremor and thinking about that. Do they have Ataxia? Do they have Neuropathy, or other things that could be related? Other aspects in terms of the history that are important, what's the response to alcohol? Generally essential tremor is very sensitive to alcohol and after somebody has one or two drinks their tremor is virtually gone so that's very helpful if you get that history. Sometimes you don't, but it can be helpful. The onset of the tremor, I'll talk a little more about that, but most people with essential tremor in their forties and then kind of this gradual worsening over time and often come to see a clinician for the first time in twenty years after their tremor started. Where in Parkinson's the average age of onset is much later being more in the sixties and they often get to a clinical referral much faster. It's not something that's usually gone on for that long. You want to ask about a family history of tremor. Again I'll talk about this a little bit more, but with essential tremor you think about that. You want to ask about what medications they're on. Could there be any medications that are worsening their tremor and were any medications started around the time when the tremor started? Also ask about drugs, of use and abuse, alcohol withdrawal. Sometimes people can get tremors so that's an important issues as well. Then associated disease, do they have Hyperthyroidism and is their thyroid off and is that causing them to shake? Do they have Diabetes and are they getting hypo-glycemic and is that causing things? So those are important aspects as well. So first of all I'm going to talk about essential tremor which is the most common etiology of tremor and the most common thing that's seen I think by a general practitioner probably. The definite criteria for essential tremor are a postural tremor in both arms that worsens with action. Its present both holding a posture and then when you actually move it tends to get worse with the movement generally. There are no other explanations for the tremor and no medical conditions that would enhance tremor or medication. So these are kind of some of the things I talked about and you look at the whole list on the slide set as well. The other form of definite is postural tremor in both arms that does not worsen with action and the presence of a head tremor. So arms and head are the most common involved in essential tremor. Again, the exclusion criteria of no medications that would be worsening it. So this is typically what a person with essential tremor, what their spiral would look like here on "A". So when they go to do this action they get this very erratic spiral, and "B" is obviously a normal tremor. Then as I said with the pouring, the cup pour is helpful. You'll find that they shake the cup and when they go to pour, the water spills all over and that would help you and also seeing an action tremor. Like I said, the upper limbs are the most classically involved. They're involved in ninety four to ninety five percent. You can have other things effected. So if the arms are effected it helps you in making a diagnosis of essential tremor, but it doesn't mean other things can't be involved. By far the next most common is head tremor and then limb less so, voice not uncommonly, tongue, face and trunk much less so. As I said with the alcohol, fifty to seventy percent of persons with essential tremor report improvement with alcohol so this is a good history if you can get it. Mean age of onset is around forty, so thirty five to forty five years of age. Often times you have to push for this a little bit. They may not have been really bothered by tremor, but if you say "When did you first notice the tremor?" it will often be many years before you're seeing them. It's autosomal dominant inherent in about sixty percent of persons so

they'll have a family history about sixty percent of the time. There seems to be a cerebellar and ataxic component that can be recognized later in life, so if an older patient comes in with essential tremor and seems to have some Ataxia as well, the two may be related. So that's not necessarily exclusionary. Typically in younger people those symptoms aren't present. The most commonly used medications are Propranolol, Primidone, Propranolol is the only one that is FDA approved, but the efficacy is pretty similar between the two. Approximately thirty percent of patients will not respond to either of those medications. For Propranolol, the doses are between thirty and 320 milligrams a day. You can use long acting preparations as well as immediately acting. Studies have found an average of about a fifty percent reduction in those that have a response. The most common side effects are light headedness, fatigue, impotence, and bradycardia. You have to be cautious with heart failure, Diabetes, or pulmonary problems. Other beta blockers can be used as well. You just have to check whether it's an essentially acting beta blocker or not. If it doesn't cross the blood brain barrier then it shouldn't have an effect on tremor, but if it does then there should be some effect. Propranolol, by far, is the most studied of them. Primidone or Mysoline is the second most commonly used treatment. Its dose range is from sixty two and a half to generally 500 milligrams, 750 milligrams, you can go up to a 10000, but usually between 500 and 750 you get pretty maximal results. Common side effects are sedation, drowsiness, fatigue, nausea, vomiting, Ataxia, malaise, dizziness, confusion, and vertigo. Generally if you increase the dose slowly these aren't a major problem. There are some patients who seem very sensitive to it and you can just never get their dose increased. Again it's about a fifty percent reduction in amplitude so pretty similar and you can use the two medications together and that's quite common in someone who has a fairly bad essential tremor to use both of them. This is a review from Neurology done in 2005. It goes through all other medications that have been looked at in terms of tremor treatment. I'm not going to go into this in too much detail. I would say Primidone and Propranolol are definitely first line, no question. Then after that Neurontin is often a good choice, Topamax is a reasonable choice, then less so from there. It may be somewhat patient dependent. So if someone's got a Neuropathy as well, Neurontin may be a good choice. If someone has Migraines, Topamax may be a good choice, but those are the primary ones that I would tend to consider.

So non-pharmacological treatments are important to think about too. One issue is because alcohol is so effective at treating the tremor, often patients use alcohol and use it quite a bit. They will sometimes have a rebound component to the tremor. So they will drink alcohol, the tremor gets better, then as the alcohol wears off their tremor actually gets worse. I've had a number of patients that when they are able to decrease their alcohol intake, their overall tremor actually seems less. So this is something important to counsel people about. Also you want to make sure they're not having problems with alcoholism because it can develop as a way to treat the tremor. Decreasing caffeine intake which can aggravate the tremor. Assistive devices can be useful sometimes. There's shaped utensils which can help, using a straw with a cup may be helpful, weighted utensils, sometimes even wearing weights on the wrists and generally the best is to refer to Occupational Therapy for assistance with these things. So there's also surgical treatment. This is a newer area and a pretty exciting area within tremor treatment because it's much more effective than the medications we have. The two options are a

Thalamotomy, or deep brain stimulation. We'll talk about those a little bit more. So a Thalamotomy involves creating a lesion so there's no hardware left behind. It's just creating a lesion within the brain. It's done within VIM, a nucleus of the thalamus, which is the Ventral Intermediate Nucleus. The things that are exciting about Thalamotomy and DBS is that the degree of improvement is much much beyond what we see with medications for the most part. As I said there's about a fifty percent reduction with the medications. There's an open label trial done and it showed eighty to ninety percent in limb tremor. As I said the effects are generally much more dramatic than medications. Thalamotomy can not be done bi-laterally. The side effects are too much of a problem. So it's generally done on one side, and that's the side opposite to the dominant hand. So if someone's left handed it would be done on the right side of the brain, if they were right handed it would be done on the left. You can do a Thalamotomy on one side and DBS on the other or just do the one Thalamotomy side which for many people, if their dominant hand is controlled, that's sufficient. The advantage over DBS is that it does not require any programming. So once the procedure is done they're done. They can go home. They don't need to come back. There's also no hardware so there's less risk of an infection associated with it. So especially for Veterans who may live in a more rural area where it's difficult for them to get in to treatment this may be a good option. So Deep Brain Stimulation is the other therapy. This is even a little bit newer than the Thalamotomy. The device is put in the same area as the Thalamotomy is done. Again the improvements are generally much more dramatic than with medications. It's a sixty to ninety percent improvement on average. There are fewer side effects than with Thalamotomy in general, but there can be more surgical complications. So that's the risk/benefit there. There can be benefit with bi-lateral or Thalamotomy for voice tremor. So if someone has a bad voice or head tremor, more central tremors in terms of the body, the bi-lateral DBS is a good option and Thalamotomy is not going to help a lot with voice tremor. Other treatments, less commonly used, but sometimes appropriate would be Botulinum toxin primarily for head tremor is where we would use it. We can paralyze the muscles that turn the head back and forth somewhat and then improve head tremor.

I'm going to show a video now. So this is a woman with a central tremor. You can see pretty dramatic tremor when she holds her hands up, and then as she moves them the tremor even gets more. She's got some tremor over her head and most prominent in her hands for sure. They show her doing a few activities. So here's that attempt at a cup pour and she's not even using both hands which we often do. You can see the water is just being spilled all over the place. Here's her spiral and you can see that it's very erratic. She's had deep brain stimulation done. She's right handed so she's had it done on the left thalamus, and it's on there. So you can see her left hand still tremors, but her right hand has much less tremor. Here she does the cup pour not spilling the water at all. They show her doing the spiral as well. Again just a very dramatic improvement. As I said with the medications the improvements don't tend to be that dramatic. So for somebody with a more severe tremor, surgical considerations are definitely an option. Generally we'll treat with Primidone, Propranolol, maybe a third medication. If that's not controlling things then a consult for surgery is a consideration. So in terms of drug induced tremors, I'm not going to spend much time on this because it's a fairly big topic, but this is a really good review. It came out in Neurology in 2005. It goes through drug induced tremors. It separates things according to the type of tremor again. Is it action or

postural? Is it in tension or is it a resting tremor? Then looks within each different category of medications of what could be a consideration. This is just a list, you can see it's pretty extensive of different medications that can cause the action or postural tremors. Then rest tremors, these are often a cause of Parkinsonism and then result in a rest tremor similar to what you see in Parkinson's. Depakote is definitely a fairly common one there. Then the neuroleptics Haldol and so forth are the most common ones and Metoclopramide probably that we see in that area. I think Cocaine as well, but we don't tend to see those patients as much in the clinic setting. Then in tension tremor Lithium is definitely a problematic one here. Ethanol we had talked about. The most helpful thing I think about picking out a drug induced tremor and how to manage it is through your history because if you look up almost any medication it's going to list tremor as a possible side effect. So figuring out whether or not in your particular patient is really the important part because so many medications can cause tremor. So was the tremor pre-existing? Enhanced physiologic tremors are the most common thing caused by a drug induced tremor so generally persons don't notice a tremor prior to being on the drug. They may have noticed if they got real nervous, they shook a little bit if they drank a lot of caffeine or some situations like that. Have other medical causes of tremor been ruled out? Again kind of the same things that I spoke about before; hypothyroidism, hypoglycemia. Is there temporal relationship to the start of a drug or an increase in the drug and the onset of the tremor. That's by far the most helpful thing in terms of sorting this out. Has the tremor worsened over time? Generally drug induced tremors do not worsen. They stay static unless the dose of the medication is being increased. Where as essential tremor in Parkinson's disease, the tremor is going to tend to worsen over time. Is the tremor bothersome? Can the medication be switched to an alternative or decreased? If someone's got a tremor, but it's not bothering them it may be very reasonable to just continue them on the medication and follow them over time. If there's an alternative medication that may end up being an option or if their medication can be decreased that would be a consideration. A less favorable step, but something that needs to be done sometimes is adding another medication to mask the tremor symptoms. Can they be put on Propranolol or Primidone to help to try to mask the symptoms, and are there other options such as adaptive equipment which could be helpful if someone is having trouble just writing can they try a bigger pen and is that going to be enough to help or can they do more typing than writing? I'm not going to use these videos. I'll go through this part of the talk and then go back to the video for Parkinson's disease. So in Parkinson's disease two of the following have to be present at least; tremor at rest, rigidity, and bradykinesia, as well as the absence of secondary causes. Often time people are going to present tremor with being their primary complaint and then you need to see if the rigidity or the bradykinesia is present as well. They can develop postural instability, but that tends to happen later on. In disease their response to medication, often dopamine agonists or Sinemet is also helpful in determining the diagnosis. Practical questions to ask a patient in the office to see if you need to be worried about Parkinson's include things like, "Does it take you longer to get dressed?" "Has your voice gotten quieter?" "Have people asked you to speak up?" "They have trouble understanding you on the phone." "Does your spouse walk faster than you now?" "Do you shuffle when you walk?" "When do you notice the tremors?" So do they say they notice the tremors when they're sitting while watching TV at night? Or do they say "It's

hard when I go to write or as I'm eating." The action is going to be much more the case with the essential tremor that "I just notice it when I'm walking or sitting" is going to be much more the case with Parkinson's. Asking if they feel stiff and also if they notice that the tremors are worse on one side. Generally with essential tremor it's pretty symmetric between the two sides. They may notice it more on their dominant hand because they're more active with that hand or as with Parkinson's it's usually clearly one side is worse than another. As I mentioned treatment briefly I'm not going to go through this too much, but generally in younger patients dopamine agonists are our first line, Requip or Mirapex being the medications that are used. I think Requip is the primary one on formulary now at the VA. They're very similar in terms of their use. Then Sinemet is generally used in older patients as our starting dose. One of the things to note here is often times I've noticed people prescribe ten one hundredths instead of twenty five one hundredths to start and as a starting dosage you really want to use the twenty five one hundredths because when you're using low doses of Levodopa you need a little bit more Carbidopa so the twenty five one hundredths should be the starting dose, not the ten one hundredths.

So let me get to the videos of Parkinson's. So this is a video of Parkinson's and you can see the very classic rest tremor here. He has got that tremor, as his hands sitting there its trembling. Then he's also got mass facies, he's kind of stooped over, he looks a little bit stiff. I think he's trying to do finger taps here. Not too obvious in the legs, but you'll often see a leg tremor on the same side. He has trouble getting up from the chair. Then you'll see as he walks it's hard for him to get started. Walking can be really helpful again for helping to distinguish the tremor. Parkinson's tremor is generally very obvious with walking, and again you can see his tremor very clearly when he walks. Where as with essential tremor it's going to be much more shown with action when it's hanging like that. Walking is not going to be such a problem. I'll show this video at the end, but the last category of tremor is a dystonic tremor. Dystonic, or Dystonia is a sustained muscle contraction which produces an abnormal posture, twisting, or repetitive movement. It's often times muscles that are doing counter motions that are contracting, so your bicep would contract when you bring your arm up and your tricep would contract for you to bring it down. In Dystonia both may be contracting so then they may be kind of fighting and then you end up with this jerky tremor type motion. Tremor is not always present. Sometimes its more of a held posture of a twisting or turning. Tremor can often result of this as I said and head tremor is the most common dystonic tremor that we see. So if someone comes in with an isolate head tremor you really want to think of Dystonia as a possibility and not just essential tremor. If they have a hand tremor as well then you'd think more towards essential tremor, but if it's just an isolated head tremor you really want to think about Dystonia. Another thing is that you want to ask with Dystonia is do they have a sensory trick. Is there somewhere you can touch that makes the tremor go away or makes your posture go away and these can be very dramatic. You may have someone who's head is severely turned to one side and they say "If I touch my cheek right here..." and they can just turn their head right back and as soon as their hand goes it's back again. It's not generally a hard pushing or anything, it's just a very slight sensory touch. The tremor tends to not be as rhythmic as with Parkinson's or with essential tremor. I have the bobble head here because it's often a bobble head type motion. It's not always in the same position and it's not as rhythmic. It's important to

distinguish these because the treatment is different. Primidone, Propranolol aren't going to help a dystonic tremor. Botulinum toxin is really the first line of treatment.

So this is a young gentleman with Torticollis or a Dystonia involving the neck. His head is turned and as you can see he has sort of this irregular motion to the head again. It's mostly a tremor left and right, but then it has some movement up as well and the head is really pulled in one direction. He's gotten Botulinum toxin injections and now you see his neck is on very straight and that there's no tremor present. Another thing with the tremor from Dystonia that can sometimes bring it out with the head tremor will help you distinguish is that they'll often say it's worse in one direction. They may notice that if they look to the left their head shakes a lot where as if they look to the right there's no tremor of their head still, where as with essential tremor it tends to tremor in all locations as well. So I think that is the end.